REMARKS

Applicants appreciate the Examiner's thorough examination of the subject application and request reconsideration of the subject application based on the foregoing amendments and the following remarks.

Claims 1-16, 14-29, 31-41, 48-50 and 55-60 are pending in the subject application, where claims 1-12, 14-19, 55-57 and 60 are withdrawn from consideration as the result of an Examiner's restriction requirement. The Examiner also indicated that a complete reply to the final rejection must include a cancellation of the non-elected claims. In view of the foregoing, Applicants reserve the right to present the above-identified withdrawn claims in a divisional application.

Claims 20-29, 31-41, 48-50, 58 and 59 stand rejected under 35 U.S.C. §103 and/or 35 U.S.C. §112, second paragraph.

As requested by the Examiner, the non-elected claims were canceled in the instant amendment without prejudice to prosecuting them in a continuing application. Claims 20, 23 and 26 were amended to add limitations thereto from the withdrawn claims being canceled in the foregoing amendment. Claim 26 also was amended to address the Examiner's non-art based rejection. The amendments to the claims are supported by the originally filed disclosure.

35 U.S.C. §112, SECOND PARAGRAPH REJECTIONS

Claim 26 stands rejected under 35 U.S.C. §112 on the grounds that there are antecedent basis, indefiniteness and/or vagueness concerns with the identified claim. Applicants respectfully traverse.

As provided above, claim 26 was amended to address the non-art concern identified by the Examiner. Applicants thus believe that the areas of rejection have been identified and addressed in the foregoing amendment.

It is respectfully submitted that for the foregoing reasons, claim 26 satisfies the requirements of 35 U.S.C. §112 and, as such, this claim is allowable.

35 U.S.C. §103 REJECTIONS

Claims 20-29, 31-41, 48-50, 58 and 59 stand rejected under 35 U.S.C. §103 as being unpatentable over the cited prior art for the reasons provided on pages 2-4 of the above-referenced Office Action. Because claims were amended in the foregoing amendment, the following discussion refers to the language of the amended claim(s). However, only those amended features specifically relied on in the following discussion shall be considered as being made to overcome the prior art reference. The following addresses the specific rejections provided in the above-referenced Office Action.

CLAIMS 20, 21, 24-29, 31, 32, 37-41, 48-50, 58 & 59

Claims 20-21, 24-29, 31, 32, 37-41, 48-50, 58 and 59 stand rejected as being unpatentable over Motamedi et al [USP 6,143,019; "Motamedi"] in view of Bryan [USP 6,410,960] for the reasons provided on pages 2-3 of the above referenced Office Action. Applicants respectfully traverse.

As to the rejection, the Office Action asserts that Motamedi teaches photodynamic therapy to treat cardiac arrhythmias and that Bryan teaches the use of MRI to locate and track the progress of tissue for photodynamic therapy. It is further asserted that it would have been obvious to employ the imaging method of Bryan in the treatment method of Motamedi, on the grounds that this is an appropriate imaging method for tracking photodynamic therapy as taught by Bryan. Alternatively, it is indicated in the Office Action that it would have been appropriate to employ the photodynamic therapy method of Motamedi in the method of Bryan. Applicants respectfully disagree with the asserted teachings of either reference as well as the combination of the references.

Applicants teach non-thermal devices and methods for the treatment and/or cure of cardiac arrhythmias. In particular, Applicants' devices and methods utilize photochemotherapy or photodynamic therapy under magnetic resonance (MR) imaging guidance. Thus, Applicants' devices and methods enable (1) photochemotherapy or photodynamic therapy for the treatment and/or cure of cardiac arrhythmias, (2) accurate positioning of the photochemotherapy or photodynamic therapy device within the cardiac chambers using MR imaging and (3) monitoring of the endpoints of the photochemotherapy or photodynamic therapy using MR imaging.

Current methods for monitoring such procedures involve X-ray fluoroscopy. These methods are lacking in several respects. Under X-ray fluoroscopy, soft tissues are not detectable and are not visible. Further, feedback is electrical rather than visual. Also, electrical feedback is not particularly reliable. Thus, Applicants' devices and methods for performing MR imaging of the treatment area is extremely useful in several ways.

First, it is important to accurately position the catheter within the cardiac chambers (*e.g.* to position the probe in the pulmonary vein orifices). Guidance in accurately placing the catheter can be based upon local anatomical landmarks and, thus, MR cardiac imaging will be particularly beneficial. Further, because the procedure takes place in the left atrium, the risk of generating emboli is of particular concern. Use of local MR imaging will allow the surgeon to watch for any coagulation on the endocardial surface. Still further, MR imaging can be used to titrate and direct therapy delivery. For example, MR imaging can be used to monitor oxygenation levels, which is particularly important in photodynamic therapy because photodynamic therapy causes increased oxygen consumption. Using MR imaging, tissue oxygen saturation can be imaged (the change from diamagnetic oxyhemoglobin to paramagnetic deoxyhemoglobin results in decreased signal intensity). This can be used to determine which tissue is affected and also to control light intensity to ensure that tissue does not become so hypoxic as to reduce free radical generation.

MR imaging can also be used to monitor phosphate levels, which is particularly important in photodynamic therapy because with photodynamic therapy, induced cellular damage, especially mitochondrial damage, rapid deterioration of ATP concentration is expected. If the mitochondrial membrane is compromised, cells have little ability to compensate for this change. Thus, MR imaging can be an excellent marker of overall cellular metabolic state and eventual response to photochemotherapy or photodynamic therapy. MR imaging can further be used to perform sodium imaging, wherein a change in sodium signal strength, which is proportional to cellular depolarization/damage, will be observed.

As was indicated in the prior Response of Applicants dated April 15, 2003, the Motamedi reference, describes a method and device for the treatment of cardiac disorders wherein the method and device (1) delivers laser light or other ablating energy intramyocardially and (2) diffuses the ablating energy over the broad area in the myocardium without causing excessive heat on the endocardial surface or in the blood pool (See col. 2, lines 39-43 thereof). It also was indicated that Motamedi does not describe or otherwise suggest a device for treating and/or curing cardiac arrhythmias comprising an illumination mechanism and an MRI receiver. Further, Motamedi does not describe or otherwise suggest a method wherein photochemotherapy or photodynamic therapy is performed using MR imaging to guide and/or monitor the procedure.

As to the assertion that Bryan teaches the use of MRI to locate and track the progress of tissue for photodynamic therapy Applicants strongly disagree. As provided in the Abstract of Bryan, as well as being clear from the discussion throughout Bryan, that invention is directed to diagnostic systems that rely on ***bioluminescence*** for visualizing tissue *in situ*. Moreover, the diagnostic systems described in Bryan are used for visualizing and detecting neoplastic tissue and specialty tissue during surgical procedures. In other words, Bryan is directed to the treatment of cancerous or neoplastic tissue. There is no indication anywhere in Bryan that the methods and techniques described therein involve the treatment or diagnosis of tissue involved with cardiac arrhythmias.

Moreover, the inventions in Bryan are all directed to the visualization or imaging of tissue using bioluminescence as the mechanism for allowing tissue to be visualized using for example night vision devices. There is no suggestion anywhere in Bryan that the inventions disclosed

therein involve imaging using magnetic-resonance imaging (MRI) techniques concurrent with the imaging processes disclosed in Bryan.

Bryan does suggest that the algorithms and computer techniques in use with known tomographic imaging techniques could be adapted so that multiple visual images obtained using the unique imaging techniques described in Bryan could be processes using the adapted/ modified algorithms and computer techniques to create slices or images from the multiply acquired bioluminescence images. It can hardly be said that this suggests using magnetic-resonance imaging (MRI) techniques concurrent with the imaging processes disclosed in Bryan.

In sum, Bryan does not teach, disclose or suggest at all the use of MRI imaging techniques nor the use of such imaging techniques as is set forth in the claims of the present invention. Moreover, there is no suggestion, teaching or motivation in Bryan to modify the methodology disclosed and taught in Motamedi so as to yield the methodology of the present invention not can one argue that such a teaching, suggestion or motivation would necessarily follow from that taught in Bryan.

It is respectfully submitted that claims 20-21, 24-29, 31, 32, 37-41, 48-50, 58 and 59 are patentable over the cited reference(s) for the foregoing reasons.

CLAIMS 22 & 23

Claims 22 and 23 stand rejected as being unpatentable over Motamedi et al [USP 6,143,019; "Motamedi"] in view of Bryan [USP 6,410,960] as applied to claim 21 and further in

view of Altman [USP 6,577,895; "reference"] for the reasons provided on page 3 of the above referenced Office Action. Applicants respectfully traverse.

As indicated in the discussion above concerning claim 21, the combination of Motamedi and Bryan does not disclose a methodology embodying the MRI and illumination techniques of the present invention. Thus, and at least for the reasons articulated above in connection with claim 21, it is submitted that claims 22 and 23 are considered to be allowable.

Also, Altman apparently is being used for the limited purposes of allegedly teaching ablating the pulmonary vein to treat cardiac arrhythmias. As such, the foregoing reasons articulated for claim 21, also apply to distinguish claims 22 and 23 from the combination of Motamedi, Bryan and Altman.

It is respectfully submitted that claims 22 and 23 are patentable over the cited reference(s) for the foregoing reasons.

CLAIMS 33-36

Claims 33-36 stand rejected as being unpatentable over Motamedi et al [USP 6,143,019; "Motamedi"] in view of Bryan [USP 6,410,960] as applied to claims 20-21, 24-29, 31, 32, 37-41, 48-50, 58 and 59 and further in view of Leone [USP 5,709,653] for the reasons provided on page 3 of the above referenced Office Action. Applicants respectfully traverse.

As indicated in the discussion above concerning claims 20-21, 24-29, 31, 32, 37-41, 48-50, 58 and 59, the combination of Motamedi and Bryan does not disclose a methodology embodying the MRI and illumination techniques of the present invention. Thus, and at least for the reasons

articulated above in connection with claims 20-21, 24-29, 31, 32, 37-41, 48-50, 58 and 59, it is submitted that claims 33-36 are considered to be allowable.

Also, Leone apparently is being used for the limited purposes of allegedly teaching a porous ballon for delivering a photodynamic therapy substance. As such, the foregoing reasons articulated for claims 20-21, 24-29, 31, 32, 37-41, 48-50, 58 and 59, also apply to distinguish claims 33- 36 from the combination of Motamedi, Bryan and Leone.

It is respectfully submitted that claims 33-36 are patentable over the cited reference(s) for the foregoing reasons.

The following additional remarks shall apply to each of the above.

As provided in MPEP 2143.01, obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. *In re Fine*, 837 F. 2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Jones*, 958 F. 2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). As provided above, the references cited, alone or in combination, include no such teaching, suggestion or motivation.

Furthermore, and as provided in MPEP 2143.02, a prior art reference can be combined or modified to reject claims as obvious as long as there is a reasonable expectation of success. *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 19866). Additionally, it also has been held that if the proposed modification or combination would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to

render the claims *prima facie* obvious. Further, and as provided in MPEP-2143, the teaching or suggestion to make the claimed combination and the reasonable suggestion of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). As can be seen from the forgoing discussion regarding the disclosures of the cited references, there is no reasonable expectation of success provided in Motamedi or Bryan. Also, it is clear from the foregoing discussion that the modification suggested by the Examiner would change the principle of operation of the device and methodology disclosed in Motamedi and/ or Bryan.

As provided by the Federal circuit, a 35 U.S.C. §103 rejection based upon a modification of a reference that destroys the intent, purpose or function of the invention disclosed in a reference, is not proper and the prima facie case of obviousness cannot be properly made. In short there would be no technological motivation for engaging in the modification or change. To the contrary, there would be a disincentive. *In re Gordon*, 733 F. 2d 900, 221 USPQ 1125 (Fed. Cir. 1984). In the present case it is clear that if the methodology or devices disclosed in either of Motamedi or Bryan were modified in the manner suggested by the Examiner it would destroy the intent, purpose or function of the device or methodology as taught by either of the references.

It is respectfully submitted that for the foregoing reasons, claim(s) 20-29, 31-41, 48-50, 58 and 59 are patentable over the cited reference(s) and satisfy the requirements of 35 U.S.C. §103. As such, these claims are allowable.

It is respectfully submitted that the subject application is in a condition for allowance. Early and favorable action is requested.

Applicants believe that additional fees are not required for consideration of the within Response. However, if for any reason a fee is required, a fee paid is inadequate or credit is owed for any excess fee paid, the Commissioner is hereby authorized and requested to charge Deposit Account No. **04-1105**.

Respectfully submitted,
Edwards & Angell, LLP

Date: May 18, 2004

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